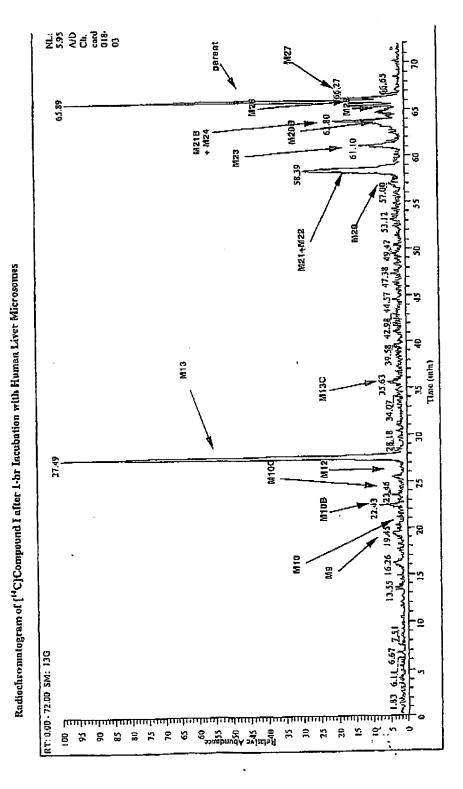
PCT/US2003/034083

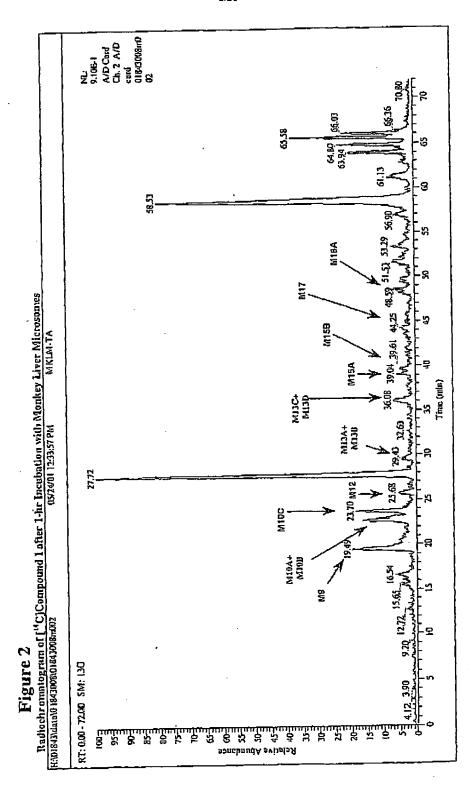
1/21



PAGE 93/113 * RCVD AT 12/5/2906 12:29:42 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/2 * DNIS:2730670 * CSID:6092524526 * DURATION (mm-ss):24-26

2/21

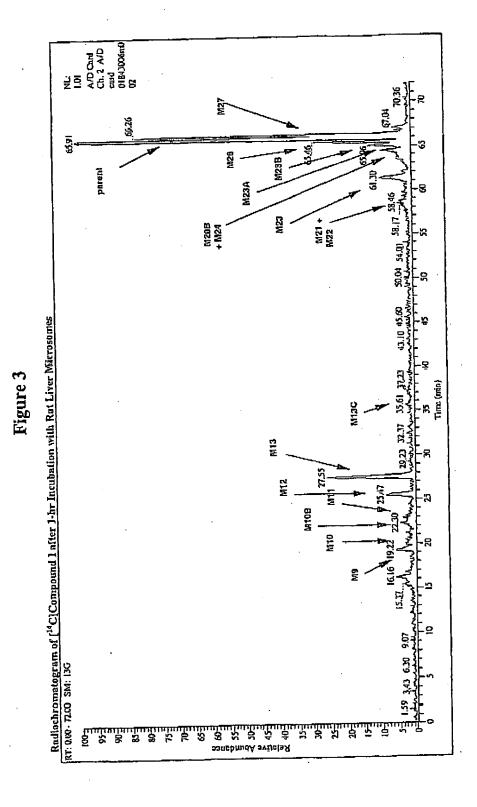
PCT/US2003/034083



PCT/US2003/034083

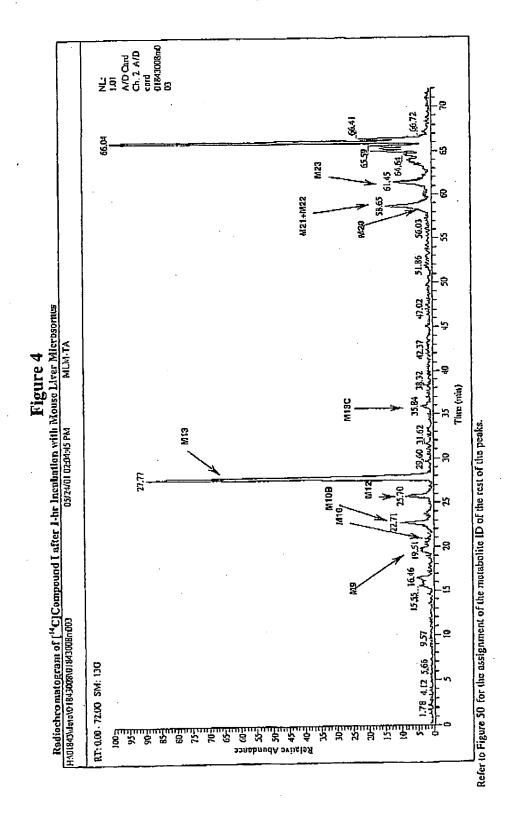
WO 2004/037211





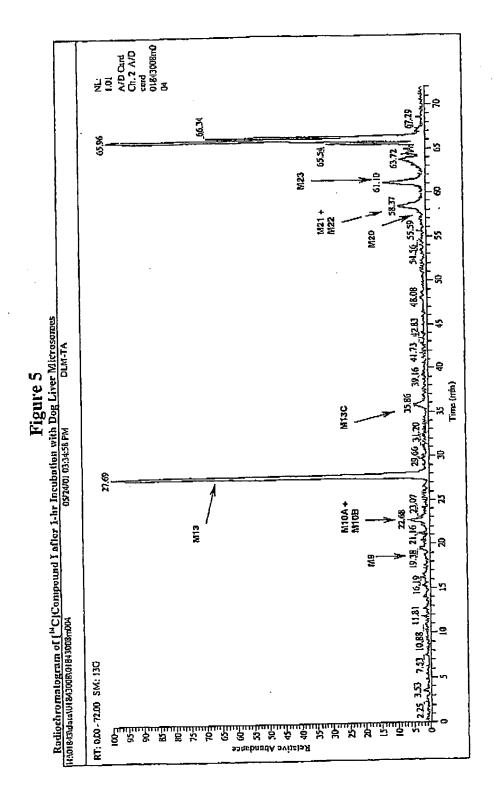
4/21

PCT/US2003/034083



5/21

PCT/US2003/034083

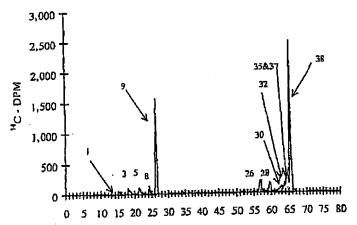


PCT/US2003/034083

6/21

Figure 6

Reconstructed HPLC Radiochromatogram of [14C]Compound I after 1-hr Incubation with Mouse Liver Microsomes



Time - Minutes

Sample Name: 01843013.002 Method: 01843

Start: 11-May-01 LSC Reference: LSC977: 101-1

ID: X977:49A (MLM-TA)

Column: Ace 5 C18, 4.6 x 250 mm, 5µm, #A3538; Guard: RP-8, 4.6 x 30 mm, 5µm

Column Temperature: 30°C

HPLC System T Detector: UV at 254 nm; 14C: Raytest

Gradiene 100% A, 3 min to 40% B, 30 min to 60% B (L5 min), 10 min to 65% B, 5 min to 100% B (9 min).
A: 0.01 M NH4OAE (nH=3 w/ HCOOH) B: Methanol Flow Rate: 1.0 ml/min

^N C Data Region No.	Metabolite	Start	Stop	R,	dpm	%ROI_	%Total
REMORTED.	, tite point	15.25	15.50	15.50	113	1.09%	0.94%
1	M9 + M10	18.00	19.25	18.00	319	3.13%	2.70%
3	м10B	21.00	23.75	21.25	266	261%	3.25%
i	M12	24.00	24.50	24.25	229	2.25%	1.94%
3	M13	26.00	27.00	26.35	2706	26.58%	23.91%
7	M20 + M21 + M22	56.25	57.75	57.00	663	6.51%	5.61%
26	M23	59.25	60.25	59.50	451	4.43%	3,82%
28	M20B + M21B + M24	61.75	63,25	63.00	410	4.03%	3.47%
30		63.50	64,00	63.75	364	3.57%	3.05%
32	M23A	64.25	64_50	64.50	551	5.41%	4.66%
15	M23B+M23C	64.75	65.00	64.75	395	3.8 9%	3,34%
37	M23D+M26	65.25	65.25	65.25	3717	36.51%	31.47%
3B	Parent DPM Recovered:	11B13		PM in ROI:	10182	100.00%	86.19%
	Di Wi Keenveleu.	11012	_				

DPM Injected: 12465 % Recovery: 94.77

Note: 1) Those peaks which accounted for >0.5% of the total were considered as ROL

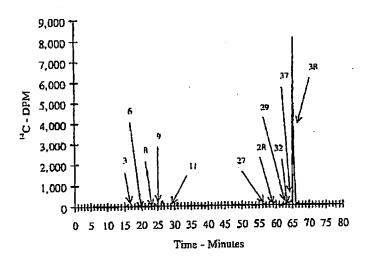
2) M13C and M27 accounted for >0.5% of the total and considered as detacted in a trace amount.

7/21

PCT/US2003/034083

Figure 7

Reconstructed HPLC Radiochromatogram of [14C]Compound I after 1-hr Incubation with Rat Liver Microsomes



Sample Name: 01843011.D03

Method: 01843

Start: 9-May-01 LSC Reference: LSC977: 82-83

ID: X977:48A (RLM-TA)

Column: Ace 5 Ci B. 4.6 x 250 mm, 5µm, #A353B; Goard: RP-B, 4.6 x 30 mm, 5µm

HPLC System T Column Temperature: 30°C

Detector: UV at 254 nm: "C: Roytest

Gradient: 100% A, 3 min to 40% B, 30 min to 60% B (15 min), 10 min to 65% B, 5 min to 100% B (9 min)

A: 0.01 M NH₂OAC (pH=3 w/HCDOH) B: Methandl Flow Rate: 1.0 mL/min

¹⁴ C Data Region No.	Membrite	Start	Stop	. R.	dpm	%ROI	%Total
3	M9+M10	18.25	19.25	18.25	183	1.29%	1.16%
6 .	M109+M11	21.00	22.00 .	21.25	151	1.06%	0.96%
8	M12	24.25	24.50	24.25	174	1.23%	1.11%
9	M13	26.25	26.75	26.50	554	3.91%	3.52%
11	11415	30.75	31.00	30.75	173	1.22%	1.10%
27	M21 + M22	56.50	57,25	56.75	159	1.12%	J.01%
27 28	M23	59.00	60.25	59.50	362	2.55%	2.30%
29	M20B + M24	62.00	63.25	62.75	212	1.49%	1.35%
	M23A	63.50	64.00	63.75	234	1.65%	1,49%
32	M23B + M26	64.25	65,00	64.75	572	4.03%	3.63%
37	poreni	65.25	66.50	65.25	11411	BD.44%	72.48%
38	DPM Recovered:	15744		PM in ROS	14185	99,99%	90.11%
	DPM Injected:	15460	_				
	% Recovery:	101.84					

Note: 1) Those peaks which accounted for >0.5% of the total were considered as ROL

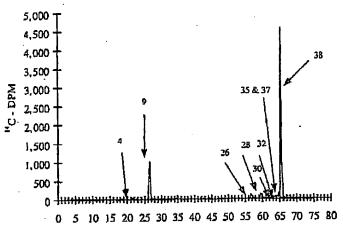
2) M13C and M27 accounted for <0.5% of the total and considered as detected in a trace amount.

PCT/US2003/034083

8/23

Figure 8

Reconstructed HPLC Radiochromatogram of [14C]Compound I after 1-hr Incubation with Dog Liver Microsomes



Time - Minutes

Sample Name: 01843013.D03 Method: 01843

S1241: 11-May-01 LSC Reference: LSC977: 114-115

ID: X977:498 (DLM-TA) Column: Ace 5 C18, 4.6 x 250 mm. 5µm. #A3538; Guard: RP-8, 4.6 x 30 mm. 5µm

Column Temperature: 30°C HPLC System T

Detector: UV at 254 nm: 16C: Raytest

Gradient: 100% A. 3 mln to 40% B, 30 rain to 60% B (15 min). 10 min to 65% B, 5 min to 100% B (9 min) A: 0.01 M NH4OAc (pH=3 w/ HCOOH) B: Methanol Flow Rate: 1.0 mL/min

¹⁴ C Data Region No.	Mstabolite	Start	Stop	R,	dpm	50ROI	%Total
4	M10A + M10B	21,25	21.50	21.50	68	0.72%	0.64%
9	M13	26.25	27.00	26.50	1807	19.15%	17.10%
76	M20 + M21 + M22	56.50	57.25	56.75	255	2.70%	2.41%
28	M23	59.25	60.00	59.50	321	3,40%	3,04%
30	M208 + M218 + M24	62.00	63.25	62.75	256	2.71%	2.42%
32	M23A	63.50	64.00	63.75	195	2.07%	1.85%
35	M23B + M23C + M25	64.25	64.50	64.25	102	1.08%	0.97%
37	M23D + M26	64.75	65.00	64.75	235	2.49%	2.22%
38	pareni	65.25	66.50	65.25	6198	65.68%	58.65%
<u> </u>	DPM Recovered:	1056B	DI	PM in ROL	9437	100.00%	89.30%
	DPM Injected	11244					

% Recovery: 93.99

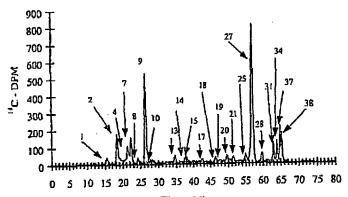
Note: 1) Those peaks which accounted for >0.5% of the total were considered as ROI. M9, M13C and M27 accounted for <0.5% of the total and considered as detected in a trace amount.

PCT/US2003/034083

Figure 9

9/21

Reconstructed HPLC Radiochromatogram of [14C]Compound I after 1-hr Incubation with Monkey Liver Microsomes



Time - Minutes

Sample Name: 01643013.D04

% Recovery: 101.65

Method: 01843 ID: X977:49C (MKLM-TA)

10-YeM-11 :1re12 LSC Reference: LSC977; 105-10

"C Data Region No.	Metabolita	Start	Ştop	r,	dpm	%ROI	%Total
		15.25	15,75	15.50	92	1.37%	[.125
	M9	18.00	20.50	18.25	5 9 I	8.80%	7.18%
2	M 10A + M 10B	20.75	22.00	21,25	367	5.46%	4.46%
1	MIOC	22.25	22.75	22,25	278	4.14%	3,38%
7	M12	24,25	24,50	24.25	61	0.91%	D.74 5 6
3	M13	26.00	27.00	25.25	1107	16.48%	13.45%
)	MIJA + MIJB	27,75	28.25	28.25	73	1.09%	0.89%
10		34.50	34.75	34.75	88	1.31%	1.07%
13	MISA	37.50	3B.00	37.75	95	1,41%	1.15%
14	MISB	38.25	38.50	38.25	56	0.63%	6.68%
15	M17	42.50	42.75	42.75	57	0.85%	Ø.69%
17		46.25	46.75	46_50	88	1,31%	1.07%
18	MISA	47.50	47.75	47.75	41	0,61%	0.50%
19	MIBB	49.25	30.50	49.75	189	2.81%	2,30%
20	M18C + M19	51.00	51.75	51.50	119	1.77%	1.45%
21	E61W + V61W	54.75	55.50	55.00	156	2.32%	1.90%
25	M20	56.00	53.30 57.75	57.00	2176	32.39%	26,44%
27	M21 + M22		60.00	59.75	137	2.04%	1.66%
28	M23	59.50		63.00	208	3.10%	2,53%
31	M21B + M24	62.75	63.50		191	2.84%	2,32%
34	M25	63.75	64.25	64.00	307	4.57%	3.73%
37	M23D + M26	64.75	65.00	64,75	-	3.60%	2.94%
38	Pprent	65.25	65.75	65.25	242		81.65%
	DPM Recovered:		D	PM in ROE	6719	100.01%	פרכיום
	DPM Injected	8097					

Note: 1) Those peaks which accounted for >0.5% of the total were considered as ROL

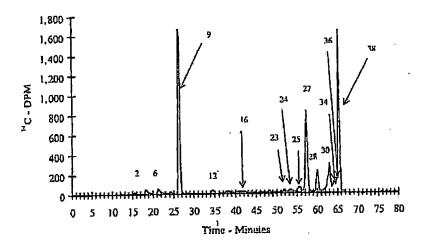
2) M27, and Regions 16, 23, and 24 accounted for <0.5% of the total and considered as detected in a trace amount.

PCT/US2003/034083

10/21

Figure 10

Reconstructed HPLC Radiochromatogram of [14C]Compound I after 1-hr Incobation with Human Liver Microsomes



Sample Name: 01843010-D02 Method: 01843

% Recovery: 102.18

State: 8-May-01 LSC Reference: LSC977: 88, 90-91

ID: X977:49D (HLM-TA)

Column: ALL S C18, 4.6 x 250 mm. Sum. #A3538; Guard: RP-8, 4.6 x 30 mm. Sum Column Temperature: 30°C

HPLC System T

Detector: UV of 254 hm; 14C: Raylest

Gradient 100% A, 3 min to 40% B, 30 min to 60% B (15 min), 10 min to 65% B, 5 min to 100% B (15 min)
A: 0,01 M NH₂OAc (pH=3 w/ HCOOH) B: Methanol Flow Rate: 1.0 mL/min

"C Data Region No.	Membalic	Start	Stop	R,	(lpm	%RO)	Total
2	M9	18.25	18.75	18,25	114	0.97%	0,85%
<u> </u>	MIOB	21.25	21.75	21.25	129	1.10%	0.96%
9	MI3	26.00	27,00	26.25	3571	30,53%	26.66%
12	MI3C	34.25	34.75	34.50	99	0.85%	0.74%
	H	41,25	42.25	42,00	112	0.96%	0.84%
16		51.75	52,25	S1.75	BB	0.75%	0.66%
23		52.75	\$4,25	53.50	168	1.44%	1,25%
24	M20	55.00	56.25	55.50	251	2.15%	1.87%
25	M21 + M22	56.50	58,25	57.25	2122	IR.14%	15.84%
27	M23	59.50	60.75	60:00	591	5.05%	4,41%
28	M208 + M21B + M24	61.25	63.50	63.00	1044	8.93%	7.79%
30	• • • •	63.75	64.50	64.00	390	3.33%	2.91%
34	M25	64.75	64.75	64.75)45	1.24%	₹80.1
36	M26	65.00	66.00	65.25	2871	24.55%	21,43%
38	paren)			PM in ROL	11695	99,99%	87.29%
	DPM Recovered:	13396	, D	FM IN ROL	11030	77.77 TP	4,123,10
	DPM Injected:	13110					

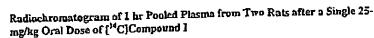
Note: 1) Those peaks which accounted for >0.5% of the total were considered as ROL.

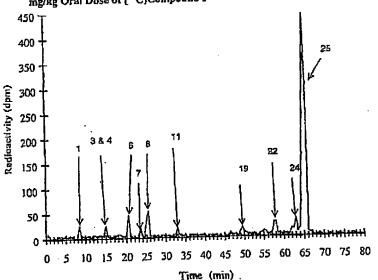
²⁾ Each of M10, M10C, M12, and M27 accounted for <0.5% of the total and considered as descened in trace amounts.

PCT/US2003/034083

11/21

FIGURE 11





Sample Name: 01842009.D02

Method: 01842

Recovery: 104.63

ID: X966:29E (Pooled Plasma, 1 hr)

Start: 3-Apr-01 LSC Reference: LSC966:84-87

Column: Acc 5 C18, 4.6 x 250 mm, 5 μm, 6A3538, Guard; RP-8, 4.6 x 30 mm, 5 μm

HPLC System T. Column temperature: 30 °C

Deterior: UV at 254 nm; HC: Roylest

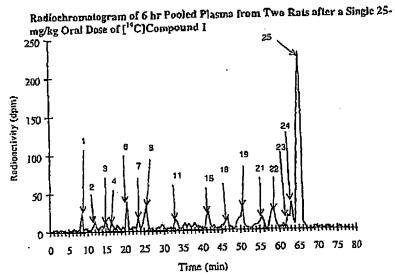
Gradient: 100% A, 3 min to 40% B, 30 min to 60% B (15 mln), 10 min to 55% B, 5 min to 100% B (15 mln) A: 0.01 M NH,OAc (pH=3 art HCOOH) B: Methanol; Flow Rate: 1.0 mL/min

Region No.	¹⁴ C Data Namo	Start	Stop	R,	dpm	%ROI	%Total
7-01		8.5	· 8.5	8.5	25	1,64%	1.35%
ı	M2		15.0	15.0	25	1.84%	1.35%
8 & 4	M7 + M8 + M8A	15.0	20.5	20.5	46	3.39%	2.48%
5	M10	20.5		23.5	22	1.62%	դ.1 9%
•	M12	23.5	23.5		96	7.07%	5.18%
\$	MI3	25.0	25.5	25.5	20	1.47%	1.08%
1	M14	33.0	33.D	33.0	19	1.40%	1.03%
9		49,5	49.5	49.5		4.20%	3.08%
22	M23	57.5	58.0	57.5	57	4.94%	3,62%
24		62_0	63.0	63.0	67	•	52.92%
25 _	earen)	64.0	65,5	65.0	980	72,72%	73.28%
	DPM Recovered:	1852		DPM in ROL	1357	99.99%	-
	DPM Injected:	1770		Note: any fraction	m consining) <u>ess</u> than 15 dpm	MP2 COUZIDES
	% Recovery:	104.63		as background a	nd not includ	led in the integral	ion.

PCT/U\$2003/034083

12/21

FIGURE 12



Sample Name: 01842009.D03

% Recovery: 112.57

Method: 01842

ID: X966:29F (Pooled Plasma, 6 hr)

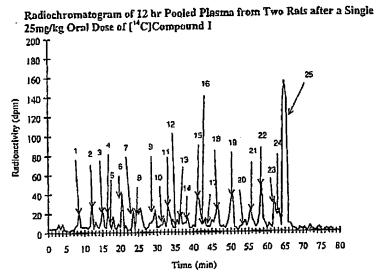
Sun: 9-Apr-01 LSC Reference: LSC966:89-92

Regian No.	¹⁴ C Data Name	Start	Siop	R,	dpm	%ROI	%Total
- 1.0.		8.5	L.5	8.5	24	2.33%	1.57%
1	M3	12.0	12.0	12,0	14	1.36%	0.91%
2		15.0	15.0	15.0	16	1.55%	1.05%
3	M7	16.5	16.5	16.5	12	1.16%	0.78%
4	M8 + M8A		20.5	20.5	38	3.69%	2.48%
6	M10	20.5	23.5	23.5	17	1.65%	1.11%
7	M12	23.5		25.5	52	5.04%	3.40%
8	M13	25.0	25.5	33.0	28	2.72%	1.83%
11	M14	33.0	33.5	41.5	43	4,17%	2.81%
15	M16	41.0	41.5	46.5	17	1.65%	1.11%
18	M19	46.5	46.5		62	6.01%	4.05%
19		49.5	50.5	50.5	17	1,65%	1.11%
21	M21 or M22	55.5	55.5	55.5 50.0	64	6.21%	4.18%
22	M23	57.5	58.5	58.0	34	3,30%	2,22%
23	M24	62.0	62.5	62.0	49	4.75%	3.20%
24		63.0	63.5	63.0			35.53%
25	parent	64.5	65.5	65.0	544	52.76%	67,34%
	DPM Recovered:	1531		DPM in ROI:	1031	100.00%	
	DPM Injected:	1360		Note: any frac	tion contain	ing less than 12	dpm was consider
	% Recovery:	112.57		as background	and not int	cluded in the into	:ខ្ពករថិ០រា.

PCT/US2003/034083

13/21

FIGURE 13



Sample Name: 01842009.D04

Method: 01842 1D: X956:29G (Pooled Plasma, 12 hr) Start: 9-Apr-01 LSC Reference: LSC966:93-96

	"Ĉ Data Name	Sun	Stop	R,	dpm	%ROI	%Total
1	M3	B.5	8.5	B.5	21	1_59%	1.11%
		12.0	12.0	12.0	28	2.12%	1.48%
2 3	M7	14.5	15.0	15.0	35	2.65%	1.85%
4	MB + MBA	16.5	16,5	16.5	21	1.59%	1.11%
5	M9	18.0	18.0	1 B.O	16	1.21%	0.84%
6	MIO	20.5	20,5	20.5	40	3.03%	2.11%
7	M12	23.5	23.5	23 <i>.</i> 5	23	1.74%	1.21%
6 7 8	M13	24.5	. 26.0	25.5	83	6.28%	4.38%
9		29.0	29.5	29.5	36	2.73%	1.90%
10		32.0	32.0	3 <u>2.</u> 0	14	1,06%	0.74%
11	M14	33.0	33,5	33.0	45	3.41%	2.37%
12	M15	35.5	3ŝ <i>.</i> 5	35 <i>-</i> 5	13	0.98%	0.69%
13		36.5	36.5	36.5	22	1.67%	1.16%
14		38.5	38,5	38.5	14	1.06%	0.74%
15	M16	41.0	42.0	41,0	87	6.59%	4.59%
16	24120	43.0	43.0	43.0	12	0.91%	0.63%
17	M18	45.0	45.D	45.0	12	0.91%	0.63%
18	M19	46.0	46.5	46.5	46	3.48%	2.42%
19	.,,,,	49.5	50.5	50.5	88	6.65%	4.64%
20		54.0	54.0	54.0	12	0.91%	D.63%
21	M21 or M22	55.0	56.0	55.5	50	3,79%	2,645
	M23	58.0	59.0	5B.5	83	6.28%	4.38%
22 23	M24	62.0	62.5	62.D	56	4.24%	2.95%
24	1477.4	63.0	63.5	63.0	40	3.03%	2.11%
25 <u>25</u>	parem	64.5	65.5	65.0	424	32.10%	22,35%
=	DPM Recovered:	1897		DPM in ROI:	1321	100.02%	69.66%
		1570		Note: 200 fee	nica con univ	ing less than 12	dpm was c

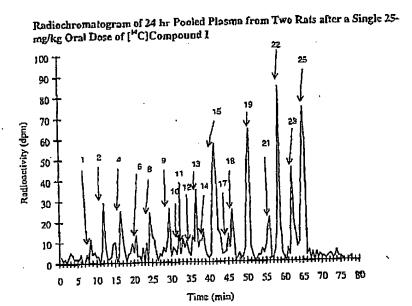
DPM Recovered: 1897
DPM Injected: 1570
% Recovery: 120.83

Note: any fraction containing less than 12 dpm was considered as background and not included in the integration.

PCT/US2003/034083

14/21

FIGURE 14



Sample Name: 01842009.D05

Method: 01842

% Recovery: 117.62

ID: K966:29H (Pooled Plasma, 24 hr)

\$18ft: 9-Apr-01 LSC Reference: LSC966:97-101

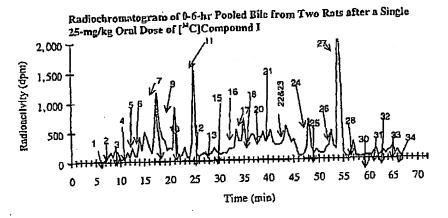
Region No.	¹⁴ C Data Name	Start	Slop	R,	dpm	%ROI	%Total
140.				B.5	11	1.10%	0.77%
1	М3	8.5	B.5	12.0	29	2.89%	2.02%
2		120	12.0	16.5	37	3.69%	2.58 %
4	M8 + M8A	16.5	17.0		13	1.30%	0.91%
6	м10	20.5	20.5	20.5	4B	4.79%	3.34%
8	M13	24.5	25.5	24.5			2,58%
9		29.0	29.5	29.5	37	3.69%	0.91%
10		32.0	32.0	32.0	13	1.30%	0.77%
iĭ	M14	33.0	33.0	33.0	11	1.10%	0.84%
12	M15	35.5	35.5	35.5	12	1.20%	2.44%
13		36.5	36.5	35.5	35	3.49%	
14		38.5	38.5	38 .5	14	1.40%	0.98%
15	M16	41.0	43.0	41.5	166	16.57%	11,57%
	M18	45.0	45.0	45.0	13	1.30%	0.91%
17	M19	46.0	46.5	46.0	38	3.79%	2.65%
18	10113	50.0	50.5	50.5)13	11.28%	7.87%
19	101 M22	55.5	56.0	56.0	38	3.79%	2.65%
21	M21 or M22	58.0	59.0	58.5	119	11.88%	8.29%
22	M23	6 2.0	63.0	62.0	80	7.98%	5.57%
23	M24		65.5	65.0	175	17.47%	12,20%
25	parent	64.5		DPM in ROI:	1002	100.01%	69.85%
	DPM Recovered:	1435		DAMINIKOL.			dpm was consid
	DPM Injected:	1220					
	-			Esakanauad	l ead not inc	this aft ni behal-	egration.

as background and not included in the integration.

PCT/US2003/034083

15/21

FIGURE 15



Sample Name: 01842006.D02 Method: 01842 (D: Pooled Bile 0-6 hr (X976:17A)

Start: 30-Mar-01 LSC Reference: X966:37-40

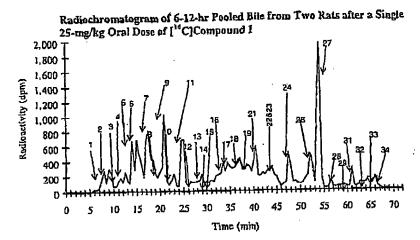
¹²C Data Region ₩ Dasc %Toral %ROI den Şum Name No. 0.16% 1.16% 1.16% 367 8.0 7.0 8.5 M1 + M2 1.49% 0.20% 473 1.50% 10.5 9.0 9.0 M4 + M5 0.12% 0.94% 0.93% 11,5 256 12.0 11.0 3 Q.18% 1.37% 436 1.38% 125 13.5 12.5 4 0.26% 1.95% 1.95% 617 14.0 14.5 14.0 М5 5 0.55% 4.11% 1303 4.12% 15.0 15.0 16,5 + MB + MBA 9.60% 9.58% 1.28% 3037 17.0 19.0 17.5 M9 203% 2025 0.27% 64 I 20.5 20.0 19.5 MID B 0.48% 3.55% 21.0 1125 3_56% 22.0 21.0 MH 9 0.20% 475 1.50% 1.50% 23.0 22.5 24.0 MI2 10 6,76% 6.74% 0.90% 2138 25.0 24.5 25.0 M13 11 1.05% 0.14% 1.06% 27.5 27.0 334 26.5 12 0.31% 2.30% 29.0 730 2.31% 30.0 28.0 13 0.15% 365 1.15% 1.15% 31.0 30.5 31.5 15 0.60% 1425 4.51% 4.49% 33.5 M14 32.D 34.0 16 0.54% 4.04% 4.05% 34.5 35.5 35.0 1282 17 M15 0.65% 4,83% 36.5 1532 4,84% 37.5 36.0 18 0.65% 4.87% 4.89% 39.0 1545 39.5 38.0 20 0.61% 4_58% 4.56% 1447 41.5 40.5 40.0 M16 21 **₽.93**₩ 1.20% 46.5 43.5 2831 8.95% 42.0 22 & 23 M17 + M18 0.52% 3.86% 1224 3.87% 48.0 49.0 M19 47.0 24 1.23% 0.16% 390 1.23% 50,5 49.5 49.5 25 0.60% 4.46% 4,45% 1412 53.5 52.5 M20 51.0 25 1.70% 12.76% 12.72% 4034 56.0 54.0 54.D 27 M22 0.25% 1.85% 1.66% 587 56.5 59.0 M23 28 0.33% 0.045 0.34% 59.5 106 59.5 60.0 30 0.16% 37D 1.17% 1.17% 62.0 61.5 60.5 M24 31 0.13% 0.95% 302 0.95% 62.5 63.5 63,0 32 1.85% 1.85% 0.25% 65.0 586 65.5 64.0 33 patent D.67% 0.09% 314 0.69% 66.0 67,0 66.0 34 31624 100.01% 99.70% 13.35% DPM in ROI: DPM Recovered:

DPM Injected: 32752 % Recovery: 96.83

PCT/US2003/034083

16/21

FIGURE 16



Sample Name: 01842606.D03 Method: 01842 (D: Pooled Bife 6-12 hr (X966:170) Sion: 30-Mar-01 LSC Reference: LSC966:41-44

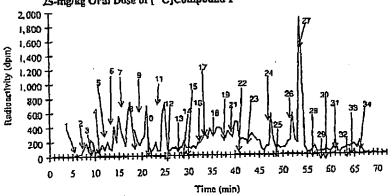
Region	¹³ C Date Name	Sum	Stop	R,	dpm	GRO I	- STotal	% Dasc
No	MI + M2	6.5	8.5	6.0	612	2,095	2.08%	0.15%
1	M4 = M5	90	10,5	4,0	573	2.32G	230%	0.15%
2	Dep on 1917s	11.0	12.0	11.5	442	1.51%	1.50%	£11.0
3		12.5	13.5	12.5	511	1.75%	1.74%	0.12%
4	M6	14.0	14.5	14.0	947	3,24%	3.22%	0.23%
5	M7 + M8 + M8A	15.0	16.5	15.D	1704	5.83%	5.79%	0.41%
6	M9	17.0	19,0	17.5	2596	8.67%	B.B2%	0.63%
7	MID	19.5	20.5	20.0	745	2.55%	153%	0.18%
B	MII	21.0	22.0	21.0	1231	4,21%	4.18%	0.29%
>	M12	22.5	24.0	23.0	504	1.72%	1.71%	0.12%
ID	MI3	24.5	26.0	25.0	1546	\$28%	5.25%	0.37%
n	14712	26.5	27.5	26.5	351	1.704	L19%	C.DBT
15		2B.0	29.3	29.0	562	1,925	1.91%	0.13%
[3		30.0	30.5	30.D	233	0.80%	0.79%	O.06%
14		31.D	31.5	31,0	260	D.89%	0.86%	Œ06%
13	MJ4	32,0	34.0	33.5	t282	4.38%	4.36%	₩£.0
16	MIS	34.5	35.5	34.5	990	3.38%	3.36%	0.24%
17	6413	36.0	37.5	37.0	1392	4.76%	4.73%	0.33%
18		38.0	39.5	38.5	1197	4.09%	4,075	0,28%
19	M16	40.0	41.5	40.5	1422	4.86%	4.83%	0.34%
2)	M17 + M18	42.0	46.D	44.0	1856	6.35%	6.31%	0.44%
22 & 23	M19	46,5	50.0	47.5	1403	4.BO%	4.77%	0.33%
24	M20	50.5	53.0	52.0	1372	4,69%	4,66%	0.73%
26	M23	53.5	35.5	54.0	3479	11.89%	11.B2S	¢.83%
27	M23	36.0	57.5	56.5	260	0.89%	0.88%	0.06%
28	1*64.2	58.0	60.0	59.0	259	0.89%	₹88,0	0.06%
29	M24	60.5	62.0	61,0	412	1,41%	1.40%	0.10%
31	M-24	62.5	63.5	63.0	273	0.935	0,93%	0.075
32		60.0	65.5	64.5	475	1.62%	1.61%	0.119
33	bareut	0.00 0.88	67.0	66.0	257	0.68%	0.87%	0.069
34	2 2 1 1 2 2			PM in ROI:	Z9253	100,00%	99,37%	6.95%
	DPM Recovered		u	rm m rot.			****	
	DPM Interest	311178						

PCT/US2003/034083

17/21

FIGURE 17

Radiochromatogram of 12-24-hr Pooled Bile from Two Rats after a Single 25-mg/kg Oral Dose of [14C]Compound I



Sample Name: 01842006.DD4 Method: 01842 (D: Pooled Bile 12-24 hr (X966:17C) Start: 30-Mur-01 LSC Reference: LSC966:45-48

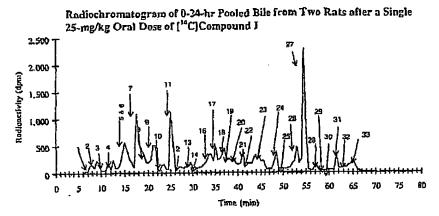
Region	¹⁴ C Data			_		# PO!	%Total	% Dose
No.	Name	Statt	Stop	R,	दीग्रम	%ROI	1.682	0.U9%
	M1+M2	6.5	8,5	B.D	434 467	1.6875 1.6176	1.80%	0.05%
2	cim ÷ Phi	9.0	10.0	9.0		1.535	1.52%	0.08%
1		ID.5	12.0	11.5	394 3 7 5	1.45%	1.45%	D.08%
2 3 4		12.5	13.5	12.5		2.25%	2.24%	0.12%
5	M6	14.0	14.5	14.0	581		4,92%	0.127%
5 6	M7 + M8 + M8A	15.0	16.5	15.0	1273	4.94%	8.61%	0.46%
7	M9	17.0	19.D	17.5	7229 633	8.65% 2.46%	2.45%	0.13%
8	M10	19.5	20.5	20.5	656	3.72%	7.315	0.137
9	M11	21.0	22.0	21.0	404	1.57%	1.56%	0.08%
10	MI2	22.5	24.D	23.D		5.64%	S.62 %	0.30%
11	M13	24.5	26.0	25.0	1454	1.15%	1.15%	0.069
12		26.5	27.5	27.0	297		1.97%	0.002
13		28.0	20.5	29.D	510	1.98%	0.80%	0.049
14		30.0	30,5	30.0	207	0.80%	0.86%	0.059
15		31.0	31.5	31.0	222 .	0.86%	4.28%	0.237
16	MJ4	32.0	34.0	33.5	1107	4.30%		0.209
17	M15	34.5	35.5	34.5	942	3.65%	3.64%	0.347
18		36.0	39.0	36.5	1642	6.37%	6.34%	
19		38.5	3 9.5	38.5	B64	3.35%	3.34%	0.189
21	M16	40.0	41.0	40.0	1093	4.24%	4, 22%	0.335
22	M17	41,5	42.5	41.5	618	2.40%	2.39%	0.139
23	MIB	43.0	46.0	43.5	1328	5.15%	5.13%	0.289
24	M19	46.5	48.\$	47.5	1087	4.22%	4,20%	0.235
25		49.0	49.5	49.0	208	0.81%	708.0	0.049
26	M20	50.0	O.£2,	52.0	1483	5.75 %	5.73%	0.315
27	M22	53.5	55.5	\$3.5	3244	12.59%	12.53%	0.689
28	M23	\$6.0	57.5	56.5	255	0.99%	0. 99 %	0.05
20 29	1.100	58.0	58.5	5B.O	93	0.36%	0.36%	0.024
		59.0	60.0	59.0	156	0.61%	0.60%	6. 031
30	M24	60.5	62.0	61.0	338	1.31%	1.31%	0.07
31	W12-4	62.5	64.0	63.5	348	1.35%	1.34%	0.07
32		64.5	65.5	64.5	359	1.39%	1.39%	0.08
33	bareut			66.0	273	1.06%	1,05%	0.05
34		66.0	67.0	PM in ROI:	25774	99.99%	99,58%	5.384
	DPM Recovered:	25882	D	PM to KOI:	25114	77.77 II	3,000	324
	OPM Injected:	26360						

% Recovery:

PCT/US2003/034083

18/21

FIGURE 18



Sample Name: 01842009.003 Method: 01842 ID: X966:288 (Pooled Bile, 0-34 hr)

Start: 3-Apr-01 LSC Reference: LSC966:80-83

Region	[™] C Dain							
No.	Мале	Ştan	Stop	R,	dpm	%ROI	୍ରାଘଟୀଙ୍କ	% Dose
1	M1 + M2	6.5	B.5	0.8	442	1.68%	1.58%	0,43%
2	M4 + M5	9.0	2.01	9.0	502	1.91%	1.90%	0.49%
3		11.0	12.0	11.5	329	1.25%	1.25%	0,32%
4		12.5	13.5	12.5	414	1.58%	1.57%	0.41%
5&6	M6 + M7 + M8 +M8A	14.0	17.0	t5.0	2311	ጺ ₽4%	5.00%	2.06%
7	MD	17.5	19.5	t7.5	2671	10.17%	10.125	2,61%
8	MIO	30.0	20.5	20.5	432	1.64%	1.64%	0.42%
9	MIL	21.0	22.5	21.0	1141	4.34%	4.32%.	1,11%
10	M12	23.0	24.5	23.5	439	1.67%	1.66%	0.43%
11	M13	25.0	26.5	25.0	1853	7.05%	7.02%	1.81%
÷2		27.0	ZR.0	27.0	312	1.19%	1.18%	0 "30₽
13		28.5	30.D	29.5	536	2.04%	2,03%	0.52%
14		30.5	31.0	30.5	182	0.69%	0.69%	0.18%
16	M14	31,5	34.5	34.0	1477	5.62%	5.60%	1,44%
17	M15	35.0	35.5	3,5.0	748	2.85%	2.84%	0.73%
18	(*****	36.0	37.5	37.0	1269	4.83%	4.81%	1.24%
19		38.0	38.5	38.0	501	1.91%	1.90%	0.49%
20		39.0	40.0	39.0	612	2.33%	2.32%	0.60%
21	м16	40.5	415	41.0	693	2.645	2.63%	0,69%
22	M17	42.0	43.0	42.0	537	2,04%	2.04%	0,53%
23	MIB	43.5	46.5	43.5	1500	5.71%	5.69%	1.47%
24	MI9	47.0	49.0	48.5	757	2.88%	2,87%	0.74%
25	14112	49.5	50.5	50.0	198	D.75%	0.75%	0.19%
26	M20	\$1.0	\$3.5	57.0	1174	4.47%	4.45%	1,15%
	M22	54.0	56.0	54.5	3444	13,11%	13.05%	3.37%
27	M23	56.5	58.0	57.0	307	1,17%	1.16%	0.30%
28	14123	58.5	59.0	5B.5	бІ	0.23%	0.23%	0.06%
29		59.5	60.5	60.0	157	0.60%	6.60%	0.15%
30	247.4	61.0	62.5	61.5	527	2.0150	2.00%	0.52%
31	M24	63.0	63.5	63.0	223	0.85%	0.85%	0.22%
32		64.0	66.5	65.0	720	2.74%	2.73%	0.70%
<u> </u>	pareni	26382	<u></u>	DPM in ROI:	26269	99,99%	\$82.00	25,67%
	DPM Recovered:	70367		Pi-lef th LCIT	20103	33.53.4		

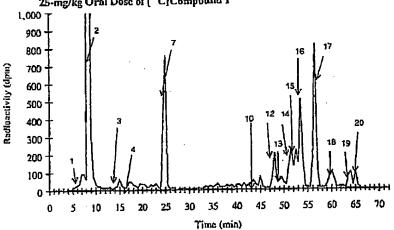
DPM Injected: 24582 % Recovery: 107.32 WQ 2004/037211

PCT/US2003/034083

19/21

FIGURE 19

Radiochromatogram of 0-12-hr Pooled Urine from Two Rats after a Single 25-mg/kg Oral Dosc of ["C]Compound I



Sample Name: 01842006.D05 Method: 01842

% Recovery:

91,16

Surt: 30-Mar-01 LSC Reference: LSC966:49-52

(D: Pooled Urine 0-12hr (X966:17D)

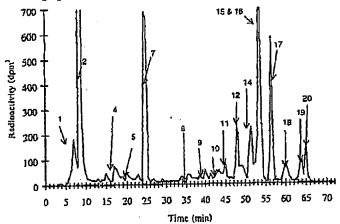
"C Data Region qbm %ROI %Tom % Dose Name Start \$10p No. 2.05% 0.06% 2.24% 7.0 310 6.0 B.0 **B223** 59.55% 54.41% 1.47% 10.0 8.5 МЭ 8.5 2 0.60% 0.02% 0.65% 90 15.5 15.0 M7 + M8 + M8A 15.0 3 1.09% 1.00% 0.03% 17,5 151 M9 17.0 18.5 4 7.8)% 0.21% B.55% M13 24.5 25.5 25.0 1181 7 1.00% 0.03% 151 1.09% 44.0 43,5 42.5 10 **M17** 2.76% 2.52% 0.07% 3B J 47.5 49.0 4B.Ô M19 12 0.02% 0.89% 49.5 135 0.98% 49.5 50.5 13 3.30% 0.09% 499 3.61% 51.0 52.0 51.5 14 0.07% 2.45% 52.5 371 2.69% 53.0 M20 52.5 15 4.7E% 4.37% 0.12% 660 M21 53.5 54.0 51.5 16 7.35% 0.20% 8.06% 56.5 1113 56.0 \$7.0 M23 17 267 1.93% 1.77% 0.05% 60.0 M24 59.0 60.5 LB 0.03% 1.15% 1.26% 64.0 174 63.5 64.0 19 0.75% 0.68% 0.02% 103 65,0 65.0 65.0 20 parent 91.36% 2,49% 15114 DPM in ROI: 13809 99.99B DPM Recovered: 16580 DPM Injected:

PCT/US2003/034083

20/21

FIGURE 20

Radiochromatogram of 12-24-hr Pooled Urine from Two Rats after a Single 25-mg/kg Oral Dose of [$^{14}{\rm C}$]Compound I



Sample Name: 01842006.D06

Start: 30-Mar-01

Method: 01842

LSC Reference: LSC966:53-56

. ID: Pooled Urine 12-24hr (X966:17E)

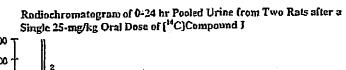
Region No.	¹⁴ C Data Name	Start	Ştop	R,	dpm	%ROI	%Total	% Dosc
1		6.0	8_O	7.0	466	3.04%	2.82%	0.03%
2	М3	8.5	10.5	8.5	6781	57.31%	53.09%	0.64%
4	М9	17.0	19.0	17.0	242	1.58%	1.46%	0.02%
5	MIO	20.0	21.0	20.0	108	0.70%	0,65%	0.01%
7	M13	24.5	25.5	24.5	1370	8.94%	8.28%	0.10%
8	M15	35.5	37.0	35_5	127	0.B35∞	0.77%	0.01%
9	M16	40.0	40.5	40.0	91	0.59%	0.55%	0.01%
10	M17	42.5	44.0	43.5	161	1.05%	0.97%	0.01%
11	M18	44.5	45.5	45.0	157	1.02%	0.95%	0.01%
12	M19	47.5	50.0	48.0	558	3.64%	3,37%	0.04%
14		51.0	52.0	51.5	456	2.9B%	2.76%	0.03%
15 & 16	M20 + M2I	52.5	54,0	53.5	1431	9.34%	8.65%	0.10%
17	M23	56.0	57.0	56.5	794	5.18%	4.80%	0.06%
18	M24	59.5	61.0	60.0	204	1.33%	1.23%	0.01%
19		63.5	64.5	64.0	196	1.28%	1.19%	0.01%
20	раселі	65.0	65.5	65.0	181	1.18%	1.09%	0.01%
	DPM Recovered:	16540		in ROI:	15323	99.99%	92.63%	1.10%

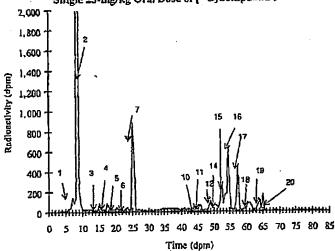
DPM Injected: 16975 % Recovery: 97.44 WQ 2004/037211

PCT/US2003/034083

21/21

FIGURE 21





Sample Name: 01842008.D02

Method: 01842

1D: X966:28A (Pooled Urine, 0-24 hr)

Stort: 3-Apr-01 LSC Reference: LSC966:76-79

Region	™C Data	.	P		dpm	%ROI	%Тош	% Dose
Np.	Name	Start	Stop	R,		2.02%	1.91%	0.07%
j.		6.0	7.5	7.0	306			
2	M3	0.8	13.0	· 8.5	8998	59.49 %	56.18%	2.19%
3	M7 + M8 + M8A	15.0	16.0	15.0	120	Q.79%	0.75%	0.03%
4	М9	17,6	19.5	17.5	238	1 <i>5</i> 7%	1.49%	0.06%
5	MIO	20.0	22.5	20.5	145	0.96%	0.91%	0.04%
6	M12	23.0	24.0	23.5	93	0.61%	0.58%	0.02%
7	MI3	25.0	26.0	25.0	1409	9,32%	8.80%	0.34%
10	M17	42.0	45.0	44.0	229	1.51%	1.43%	0.06%
	1410	45.5	46.0	46.0	118	0.78%	0.74%	0.03%
11	. M19	48.5	49.5	49.0	201	1.33%	1.25%	0.05%
12	MITA	50.0	51.5	ک.50 ک.50	209	1.38%	1.31%	0.05%
14	1420	52.0	<i>5</i> 3.0	525	476	3.15%	2,97%	0.12%
15	M20	\$3,5	56.0	54.5	1197	7.91%	7.47%	0.29%
16	MZI					4.16%	3.93%	0.15%
17	M23	56.5	58.0	57.5	629			0.09%
18	M24	59.0	62.5	61.0	356	2.35%	2.22%	
19		0.63	64.5	64.0	331	1.53%	1.44%	0.06%
20	parent	65.0	65.0	65.0	169	1.12%	1.06%	0.04%
	DPM Recovered:	16015		DPM in ROI:	15124	99.98%	94.45%	3.69%

DPM Injected: 17175 % Recovery: 93.25